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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Jonathan McKinno Collins

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SUMMA, ALLAN & ADDITON, P.A.
11610 NORTH COMMUNITY HOUSE ROAD
SUITE 200
CHARLOTTE, NC 28277

EXAMINER

CORDERO GARCIA, MARCELA M

ART UNIT

PAPER NUMBER

1654

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/604,022	Applicant(s) COLLINS ET AL.	
	Examiner Marcela M. Cordero Garcia	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on August 16, 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-61 is/are pending in the application.
- 4a) Of the above claim(s) 13-61 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is in response to the reply received on August 16, 2006.

Claims 1-61 are pending in the application. Claims 13-61 are withdrawn as not drawn to the elected Group.

Any rejection from the previous office action, which is not restated here, is withdrawn.

Applicant has now amended the base claim to recite synthesis in a single vessel. Claims 1-12 are presented for examination on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless—

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 4 are rejected under 35 U.S.C. 102(b) as being anticipated by Martin et al. (US 2003/0082633) as evidenced by Hilpert et al. (Protein Engineering, 2001).

Martin et al. teach a process for the solid phase synthesis of peptides (EQKLISEEDL and EQKHISEEDL) in a single vessel (e.g., Example 12-13) and shortening reaction times by a factor of 2-20 fold by the use of the microwave energy during the reactions (e.g., Example 12, [0294]-[0300]). Hilpert et al. teach that the

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peptides of Martin et al. were synthesized via a cellulose-bound C-terminus with two β -alanine as a spacer (e.g., column 2, lines 16-18) and following a protection/deprotection scheme (e.g., column 2, lines 12-17) and therefore would inherently encompass the instantly claimed standard solid phase peptide synthetic steps. Please note that the limitation "in a single vessel without removing the peptide from the single vessel between cycles" is met by the fact that the peptides are chemically bound to the cellulose during synthesis as taught by Hilpert (e.g., column 2, lines 8-9, 16-18).

Therefore, the reference is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4 and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004) in view of Williams (US 6,858,434) and in view of Martin et al. (US 2003/0082633).

Yu et al. teach a process for the solid phase synthesis of peptides, which comprises:

(a) deprotecting a first amino acid linked to a solid phase resin by removing protective first chemical groups;

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(b) activating chemical groups on a second amino acid to prepare the second amino acid for coupling with the first amino acid;

c) coupling the activated second amino acid to the deprotected first amino acid to form a peptide from the first and second amino acids; and

(d) accelerating at least the coupling step by applying microwave energy during the coupling step. (see, e.g., page 4782-4784, Figures 1-2 and Scheme 1).

Yu et al. do not teach accelerating the deprotecting step by applying microwave energy during the deprotecting step or carrying out the reaction in a single vessel without removing the peptide from the single vessel between cycles.

Williams teaches deprotecting n-Boc protected amino acids by applying microwave energy during the deprotecting step (e.g., Example 5).

Martin et al. teach a process for the solid phase synthesis of peptides (EQKLISEEDL and EQKHISEEDL) in a single vessel using microwaves (e.g., Example 12).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the solid phase microwave method of Yu et al. by carrying out the reaction on a cellulosic membrane to which the peptide to be synthesized is attached, as taught by Martin et al. (See, e.g., [294]-[301]) and accelerating the synthesis steps including deprotecting steps (as taught by Williams) with microwaves (See, e.g., Martin et al., column 23, [294]-[301]). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in comparison to conventional heating methods--

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substantially accelerate reactions and save time as taught by Yu et al. (page 4781, column 1, lines 13-15) and by Williams (Example 5). There would have been a reasonable expectation of success, given the successful synthesis in a single vessel of the peptides: EQKLISEEDL and EQKHISEEDL as taught by Martin et al. (e.g., Examples 12-13). Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 5, 9-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yu et al. (J Org Chem 1992, citation 6 in the IDS of June 7, 2004) (Tetrahedron Letters, 2001) in view of Stadler et al. (Eur J Org Chem, 2001) in view of Santagada et al. (Tetrahedron Letters, 2001, citation 4 in the IDS of November 8, 2004) and in view of Martin et al. (US 2003/0082633).

Yu et al., Williams and Martin et al. are relied upon as above.

Yu et al. do not expressly teach accelerating the deprotecting step by applying microwave energy during the deprotecting step, maintaining the peptide in a single vessel during the process proactively cooling the vessel and its contents during application of microwave energy, cleaving the peptide from the resin applying microwave energy, deprotecting side chains of the peptide, spiking the microwave energy, using phosphonium activators, uranium activators, HATU, HBTU, PyBOP, PyAOP or HOBT, monitoring the temperature of the vessel and moderating the applied power accordingly.

Stadler et al. teach cleaving various molecules including carboxylic acids from resins by applying microwave energy, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power accordingly (see, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2).

Santagada et al. teach using PyBOP/HOBt and HBTU/HOBt activators in a microwave method for peptide synthesis (see, e.g., pages 5171-5173).

Martin et al. teach a process for the solid phase synthesis of peptides (EQKLISEEDL and EQKHISEEDL) in a single vessel using microwaves (e.g., Example 12).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the microwave method of Yu et al. by also accelerating the deprotecting steps in general during peptide synthesis with microwaves based on the teachings of Williams (See, e.g., Examples 5 and 7), by accelerating the cleavage from the solid-support resin as taught by Stadler et al. (See, e.g., page 922, column 2, paragraph 2; page 923 and Scheme 2, page 924, columns 1-2), and by using activators such as PyBOP/HOBt and HBTU/HOBt during microwave activation, spiking the microwave energy, proactively cooling the vessel and monitoring the temperature of the vessel, moderating the applied power accordingly, as taught by Santagada et al. (See, e.g., pages 5171-5173). The skilled artisan would have been motivated to do so because it was known in the art that microwave-driven synthetic methods --in comparison to conventional heating methods-- substantially accelerate reactions and save time (e.g., Yu et al. page 4781, column 1, lines 13-15) and provide higher yields

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(e.g., Santagada et al. abstract). There would have been a reasonable expectation of success, given the successful synthesis in a single vessel of the peptides:

EQKLISEEDL and EQKHISEEDL as taught by Martin et al. (e.g., Examples 12-13). The adjustment of particular conventional working conditions (e.g., deprotecting protective groups other than n-Boc in peptides, and alpha-amino groups or side chains of the peptide) is deemed merely a matter of judicious selection and routine optimization that is well within the purview of the skilled artisan.

Thus the invention as a whole was clearly prima facie obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcela M. Cordero Garcia whose telephone number is (571) 272-2939. The examiner can normally be reached on M-Th 7:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Marcela M Cordero Garcia, Ph.D.
Patent Examiner
Art Unit 1654

MMCG 12/06


ANISH GUPTA
PRIMARY EXAMINER